REMARKS

Claims 1-25 were pending in this application; of those claims 1-25 have been rejected. Claims 1-16, 18 and 21-25 have been amended. New claims 34-36 have been added to particularly point out and distinctly claim embodiments of Applicant's invention. No new matter has been added, and support for claims 1-16, 18, 21-25 and 34-36 can be found throughout the specification, for example, at page 34, lines 13-23; page 36, lines 19-32; page 39, lines 17-23; page 40, line 15 through page 43, line 5 and FIG. 7.

Rejections under 35 USC § 103(a)

A. Claims 1, 3, 5-12 15-20, 24 and 25 stand rejected as allegedly being unpatentable over Schubler et al. (TIG, 1995, 11, 378-379) ("Schubler") in view of U.S. Patent 6,723,510 to Lubenow et al. ("Lubenow").

According to the Office Action, Schubler teaches a sequential method of isolating nucleic acid and proteins from tissue samples. The method involves first isolating poly(A)$^+$RNA from the sample using magnetic olido(dT) particles. In a second step, DNA or protein is extracted from the supernatant after removal of the poly(A)$^+$RNA by precipitation followed by centrifugation to leave a pellet of DNA or protein and supernatant.

As acknowledged by the Examiner, Schubler does not disclose binding proteins to a solid support by effecting a chromatographic interaction or that the solid support is in the form of magnetic particles.

Lubenow has been provided for its teaching of oligodT magnetic particles for binding polyA RNA and magnetic particles for protein isolation comprising ion exchange resins, hydrophobic interaction resins or nickel-nitrilotriacetic acids, where Example 1, column 2, lines 15-37 and column 10, lines 15-42 have been provided for support.

The Examiner is of the position "it would have been prima facie obvious to one of having the ordinary skill in the art at the time the claimed invention was made to modify the protein isolation method of Schubler et al with the magnetic solid supports for the protein isolation method of Lubenow et al. with a reasonable expectation of success."

Applicants note that a threshold requirement for establishing a *prima facie* case of obviousness with regards to claim 1 is that all elements of the rejected claim(s) must be found in the combination of Schubler and Lubenow (see, MPEP §2143).

Claim 1, as amended, recites, "wherein nucleic acid components bind to the plurality of first particulate solid supports in a sequence independent manner" (Emphasis added).

The combination of Schubler and Lubenow does not teach or suggest at least this limitation in claim 1. Rather, both cited references disclose the use of sequence dependent isolation methods. As described above, Schubler teaches isolation of poly(A)$^+$RNA from the sample using magnetic oligo(dT) particles. The interaction of the poly(A)$^+$ tail of RNA with oligo(dT) is a sequence dependent interaction based on the hybridization of adenosine (A) of the RNA and thymidine (T) residues of the capture sequence on the particle. This is contrary to the assertion on page 3 of the Office Action that "nucleic acid components in the sample are bound to solid support in a sequence independent manner." Lubenow, which only generally mentions the possibility of using affinity interactions for isolation of nucleic acids, also does not provide any specific example of a material that could be used for sequence independent isolation of nucleic acids. Rather, the affinity materials proposed by Lubenow for capture of nucleic acids rely on sequence dependent interactions, namely, "oligo-dT for binding polyA tails of mRNA and nucleic acid polynucleotides for binding complementary polynucleotides" (see, col. 10, lines 30-32). Therefore, Lubenow does not remedy the deficiency of Schubler, as the reference does not disclose sequence independent binding of nucleic acid components to a solid support.

In addition, claim 1 has been amended to recite:

"contacting the sample with a plurality of second magnetic particulate solid supports distinct from the first particulate solid supports, wherein protein components contained in the sample bind to the plurality of second particulate solid supports through a chromatographic interaction; and

separating the plurality of first particulate solid supports to which are bound nucleic acid components and the second plurality of particulate solid supports to which are bound protein components from unbound components in the sample."

As noted above, Schubler does not teach or suggest binding proteins to a magnetic solid support by a chromatographic interaction. Schubler also does not teach separating the particulate solid supports to which are bound nucleic acid components and the particulate solid supports to which are bound protein components from unbound components in the sample.

Lubenow, although broadly disclosing the possibility of using affinity beads for protein and nucleic acid isolation, does not teach or disclose isolation of nucleic acid and protein components from a sample using a multi-step process. Further, Lubenow does not teach or suggest contacting the sample with two distinct types of magnetic particulate solid supports, where nucleic acid components bind to the first type of solid support and protein components bind to the second type of solid support or separating the two types of solid supports from unbound components in the sample after binding. For at least these reasons, Lubenow fails to remedy the deficiencies of Schubler. Since the combination of cited references fails to teach or suggest all limitations of claim 1, as amended, a *prima facie* case of obviousness has not been established with respect to claim 1. Claims 2-25 depend either directly or indirectly from claim 1 and are, therefore, allowable for at least the same reasons as those provided above with respect to claim 1. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a).

B. Claims 1, 2 and 22 stand rejected as allegedly being unpatentable over Schubler et al. (TIG, 1995, 11, 378-379) ("Schubler") in view of U.S. Patent 6,723,510 to Lubenow et al. ("Lubenow") as applied to claim 1 and further in view of U.S. Patent 6,218,531 to Ekenberg et al. ("Eckenberg").

The Office Action acknowledges that Schubler and Lubenow (discussed above) do not teach that DNA and RNA are bound to the same solid support. According to the Office Action, however, Eckenberg teaches a method for isolating nucleic acids wherein DNA and RNA are bound to the same solid support (i.e., silica matrix) in the presence of a detergent and further teaches that the silica matrix is in the form of magnetic beads. The Office Action concludes that it would have been prima facie obvious to one having the ordinary skill in the art at the time the claimed invention was made to modify the nucleic acid isolation method of Schubler with the magnetic solid supports for isolating DNA and RNA of Ekenberg with a reasonable expectation of success.

Applicants traverse this rejection for the reasons set forth below.

As discussed above, Schubler and Lubenow, either alone or in combination, fail to teach or suggest the method of claim 1.

Ekenberg is directed to a method for isolating RNA from a biological sample using a silica-based matrix. In the Ekenberg method, a biological sample containing DNA, RNA and proteins is lysed and treated with a dilution buffer causing the DNA and protein "drop out of solution in the form of a precipitate." (see, col. 13, lines 1-11). The cleared lysate solution containing RNA and DNA then is placed in contact with a silica matrix, and the matrix is subsequently treated with DNase to digest DNA bound to the matrix.

Ekenberg does not teach or suggest that protein components in the biological sample should be contacted with magnetic particulate solid supports or that the protein components bound to the supports are separated from unbound components in the sample. Thus, the teachings of Ekenberg fail to remedy the deficiencies of the combination of Schubler and Lubenow. In view the above, Applicants respectfully submit that a *prima facie* case of obviousness has not been established with respect claim 1, 2 or 22. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a).

C. Claims 1, 3-4, 13-14, 21 and 23 stand rejected as allegedly being unpatentable over Schubler et al. (TIG, 1995, 11, 378-379) ("Schubler") in view of U.S. Patent 6,723,510 to Lubenow et al. ("Lubenow") as applied to claim 1 and further in view of Safarik et al. (Allen et al. Editors, Academic Press, 2000, pgs. 2163-2170) ("Safarik").

According to the Office Action, it would have been prima facie obvious to one having the ordinary skill in the art at the time the claimed invention was made to modify the magnetic support nucleic acid isolation method of Schubler (discussed above) with magnetic solid supports using the variety of affinity reagents taught in Safarik with a reasonable expectation of success.

Applicants traverse this rejection for the reasons set forth below.

As discussed above, Schubler and Lubenow, either alone or in combination, fail to teach or suggest all limitations of claim 1.

Safarik provides a review of the field of isolation and separation of molecules using magnetic particles. Various examples of magnetic particles are provided by Safarik for use in magnetic affinity separations of nucleic acids and proteins (see, e.g., Table 1 and Table 3). Safarik, however, does not teach or suggest using magnetic particles for isolating nucleic acid

and protein components from a sample using a multi-step process, as described in claim 1. In particular, Safarik does not contemplate contacting a sample with two distinct types of magnetic, particulate solid supports to separately bind nucleic acid and protein components and then isolating the two types of supports from the unbound components in the sample. As such, Safarik does not remedy the deficiencies of the combination of Schubler and Lubenow.

For at least these reasons, Applicants respectfully submit that a *prima facie* case of obviousness has not been established with respect claims 1, 3-4, 13-14, 21 and 23. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above amendment and remarks, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (541) 335-0070.

Respectfully submitted,

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